

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 61, 63-90, 92-122 are pending in the application, with claims 61 and 90 being the independent claims. Support for these amendments can be found, *inter alia*, on page 8, lines 9-12; and in the Examples, specifically page 26, lines 29-33; page 32, lines 20-36; page 34, lines 7-11; page 35, lines 3-13; and page 39, lines 15-17. Support for new claims 121 and 122 can be found, *inter alia*, on page 8, lines 10-12 and in the examples. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 102(e)

For rejections under 35 U.S.C. § 102, the Federal Circuit held "[a] claim is anticipated only if *each and every element* as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 613, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (emphasis added).

Brann

Claims 61, 63-64, 67-71, 74-85, 87-90, 92-93, 96-100, 103-114, and 116-120 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Brann (WO

95/02823). The Examiner alleged that Brann teaches a high throughput parallel screening method of determining the pharmacological effect of a test substance on the activity of more than one receptor molecules in test cells of the same type. Applicants respectfully traverse this rejection as it may apply to the amended claims.

Claims 61 and 90 have been amended to include a step for selecting from a cell population the test cells containing the target molecule then applying the test substance to the selected cells. In claims 121-125, the selection step further described as clonal selection or antibiotic (G418) selection. This selection step ensures that the majority of the test cells contain the target molecule, whereas Brann specifically requires a *low* percentage of cells containing the target molecule so as to allow measurement of the relative growth of responsive cells as compared to the background of cells without the target molecule. Brann, page 19, lines 27-35; page 23, lines 13-15. Brann discusses in detail this competitive growth of the transfected cells in the mixture of transfected and untransfected cells on page 6, line 23 through page 7, line 20. Further, Brann states an advantage of their method is that no control cell lines are required. *See* page 9, lines 27-28. Therefore, Brann absolutely requires that the percentage of test cells containing the target molecule be low when the ligands are added to be able to measure a growth competition against the nontransfected cells, in sharp contrast with the instant method in which the test cells are selected to contain the target molecule prior to application of the test substance.

Further, as a way of controlling the receptor number per cell in the Multiple Receptor Format of the Brann method, only a minority of the tested cells are transfected by using a low concentration of DNA. Brann, page 27, lines 23-28 and Figure 10. Thus,

the Brann method requires that only a minority of test cells contain the target molecule to distinguish different receptor activities, as well as relative growth which is in direct opposition to the instant claims, which achieve a high percentage of cells containing the target molecule prior to the addition of the test substance. Brann in no way teaches selecting for test cells containing the target molecule prior to the addition of the test cell; instead, it teaches away from such a selection step. Therefore, Brann does not teach each and every element of the claims and cannot anticipate the claimed invention. Applicants respectfully request that the rejection be withdrawn.

Applicants also note that claim 90 and its dependents require that the test cells be of a different type (or activation/differentiation state) and also contain the same target molecule. The Examiner does not point to any passage in Brann that teaches a method using this arrangement of test cells, nor does reading Brann reveal any such method. Brann exclusively teaches the use of a single cell type transfected with one or more receptor and/or markers. Even in the multiple receptor assay, the same cell types are transfected, then divided into several identical aliquots for screening with different test substances. *See, e.g.*, page 25, lines 14-29. For this additional reason, Brann cannot anticipate claim 90 and its dependents, and Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. § 103

In re Vaeck (947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)), outlines the factors required for establishing a prima facie case for obviousness: prior art references that teach all claim limitations, a motivation to combine the teachings in the references

themselves or knowledge known to a person of skill in the art at the time the invention was made, and a reasonable expectation of success from the combination of elements in the references. As discussed below, Applicants respectfully assert that these requirements have not been met to support a *prima facie* argument for obviousness for the instant claims.

Brann in view of Chalfie

Claims 86 and 115 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Brann in view of Chalfie. Specifically, the Examiner asserted that the alleged parallel screening method of Brann and the green fluorescent protein (GFP) of Chalfie render the listed claims obvious. Applicants respectfully traverse this rejection.

The deficiencies of Brann have been discussed *supra*. As discussed in Applicants' previous Reply, Chalfie merely teaches the use of GFP as a reporter gene. It does not teach the high throughput parallel screen of the instant claims or remedy any of the specific deficiencies of Brann. Therefore, since this combination of references does not teach each and every element of the claims, Applicants assert that the Examiner has not met the burden for a *prima facie* case for obviousness. Applicants respectfully request that the rejection be withdrawn.

Brann in view of Reed

Claims 65 and 94 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Brann in view of Reed. Specifically, the Examiner asserted that the alleged parallel screen of Brann combined with the BAP and Bcl-2-related solid-phase protein binding

assays of Reed render the listed claims obvious. Applicants respectfully traverse this rejection.

The deficiencies of Brann have been discussed *supra*. As discussed in Applicants' previous Reply, Reed describes a binding assay of proteins fixed to a solid support (*see* Figure 7 and Example VII). It does not teach the high throughput parallel screen of the instant claims or remedy any of the specific deficiencies of Brann. Therefore, since the combination of Brann and Reed does not teach each and every element of the claims, Applicants assert that the Examiner has not met the burden for a *prima facie* case for obviousness. Applicants respectfully request that the rejection be withdrawn.

Brann in view of Brown

Claims 66, 72-73, 95 and 101-101 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Brann in view of Reed. Specifically, the Examiner asserted that the alleged parallel screen of Brann combined with the target molecules of HER, KDR and Raf receptors allegedly taught by Brown rendered the listed claims as obvious. Applicants respectfully traverse this rejection.

The deficiencies of Brann have been discussed *supra*. Brown does not overcome these deficiencies as it merely tests the effects of certain drugs on stimulation of untransfected cells by certain growth factors. The burden of a *prima facie* case for obviousness has not been met as no combination of Brann in view of Brown would arrive at the claimed invention. Thus, Applicants respectfully request that the rejection be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Victoria S. Rutherford

Victoria S. Rutherford, Ph.D.

Agent for Applicants

Registration No. 52,253

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1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

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